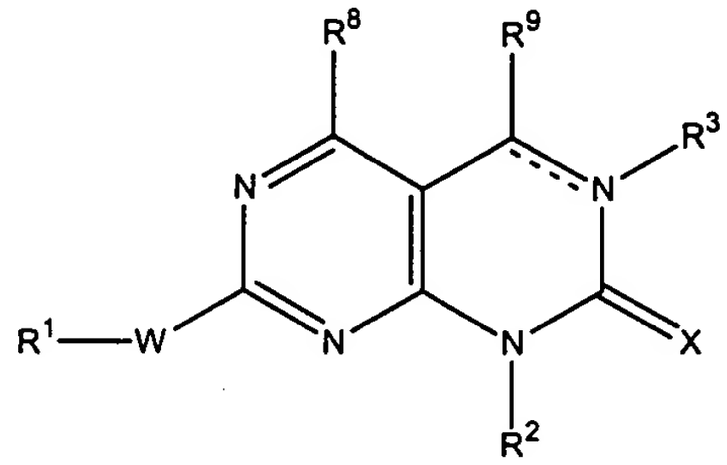
APPENDIX 1 CLEAN COPY OF AMENDED CLAIMS

54. A compound of Formula I



I

or a pharmaceutically acceptable salt thereof,
wherein:
the dotted line represents an optional double bond;
W is NH, S, SO, or SO_2;

X is either O, S, or NR^{10};
R^1, R^2, and R^{10} are independently selected from the group consisting of H, $(CH_2)_nAr$, COR^4, $(CH_2)_n$heteroaryl, $(CH_2)_n$heterocyclyl, C_1-C_{10} alkyl, C_3-C_{10} cycloalkyl, C_2-C_{10} alkenyl, and C_2-C_{10} alkynyl, wherein n is 0, 1, 2, or 3, and the $(CH_2)_nAr$, $(CH_2)_n$heteroaryl, alkyl, cycloalkyl, alkenyl, and alkynyl groups are optionally substituted by up to 5 groups selected from NR^4R^5, $N^+(O)R^4R^5$, $N^+R^4R^5R^6Y^-$, alkyl, phenyl, substituted phenyl, $(CH_2)_n$heteroaryl, hydroxy, alkoxy, phenoxy, thiol, thioalkyl, halo, COR^4, CO_2R^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4, aldehyde, nitrile, nitro,
heteroaryloxy,

$$T(CH_2)_mQR^4,\ T(CH_2)_mC(OR^5)H\text{-}(CH_2)_mQR^4,$$

$C(O)T(CH_2)_mQR^4$, $NHC(O)T(CH_2)_mQR^4$, $T(CH_2)_mC(O)NR^4NR^5$, and $T(CH_2)_mCO_2R^4$ wherein each m is independently 1-6, T is O, S, NR^4, $N^+(O)R^4$, $N^+R^4R^6Y^-$, or CR^4R^5, and Q is O, S, NR^5, $N^+(O)R^5$ or $N^+R^5R^6Y^-$;

and additionally alkyl, alkenyl and alkynyl can be further substituted with one to three cycloalkyl groups,

when the dotted line is present, R^3 is absent;
otherwise R^3 has the meanings of R^2, wherein R^2 is as defined above, as well as OH, NR^4R^5, $COOR^4$, OR^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4,
$T(CH_2)_mQR^4$, or

$$T(CH_2)_mC(OR^5)(H)-(CH_2)_mQR^4,$$

wherein T and Q are as defined above;
R^4 and R^5 are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, substituted alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $N(C_1$-C_6alkyl$)_{1 \text{ or } 2}$, $(CH_2)_nAr$, C_3-C_{10} cycloalkyl, heterocyclyl, and heteroaryl, or R^4 and R^5 together with the nitrogen to which they are attached optionally form a ring having 3 to 7 carbon atoms and said ring optionally contains 1, 2, or 3 heteroatoms selected from the group consisting of nitrogen, substituted nitrogen, oxygen, and sulfur;
when R^4 and R^5 together with the nitrogen to which they are attached form a ring, the said ring is optionally substituted by 1 to 3 groups selected from OH, OR^4, NR^4R^5, $(CH_2)_mOR^4$, $(CH_2)_mNR^4R^5$, $T\text{-}(CH_2)_mQR_4$, $CO\text{-}T\text{-}(CH_2)_mQR^4$, $NH(CO)T(CH_2)_mQR^4$, $T\text{-}(CH_2)_mCO_2R^4$, and $T(CH_2)_mCONR^4R^5$;
R^6 is alkyl;
R^8 and R^9 independently are H, NR^4R^5, $N^+(O)R^4R^5$, $N^+R^4R^5R^6Y^-$, COR^4, CO_2R^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4, CN or nitro;

when the dotted line is absent, R^9 can additionally be = NOH ,

= NOalkyl , =NOalkenyl, =NOalkynyl or =NOcycloalkyl;
and

Y is a halo counter-ion;

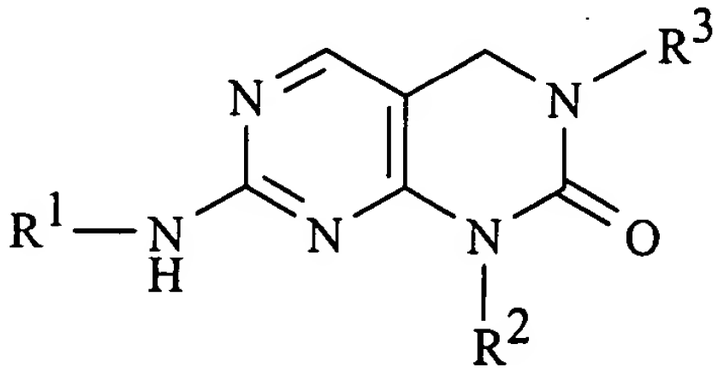
with the proviso that: (a) when R^8 and R^9 are both hydrogen, W is NH, R^1 is hydrogen and X is NR^{10}, then R^{10} is neither unsubstituted (C_1-C_{10}) alkyl, unsubstituted (C_2-C_{10}) alkenyl nor unsubstituted (C_2-C_{10}) alkynyl;

(b) when R^8 or R^9 is NR^4R^5, $N^+(O)R^4R^5$, or $N^+R^4R^5R^6\ Y^-$, then one or more of R^4, R^5 and R^6 must be, independent of the nitrogen to which said one or more R^4, R^5 and R^6 are attached, heterocyclic or heteroaryl; and

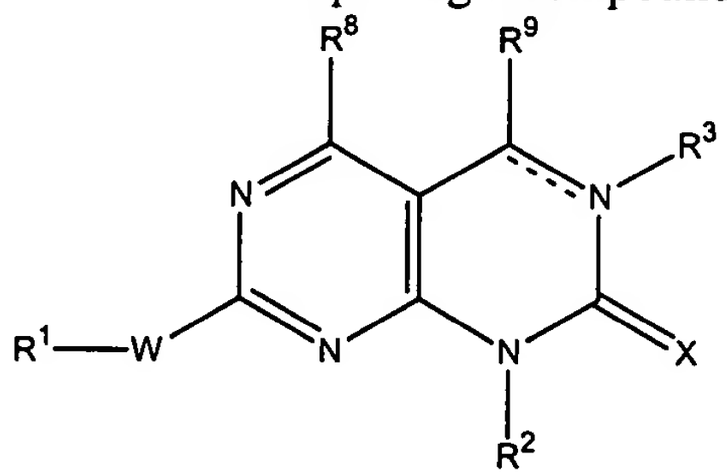
(c) when R^8 or R^9 is COR^4, CO_2R^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4 or PO_3R^4, then one or more of R^4, R^5 and R^6 must be, independent of the nitrogen to which said one or more R^4, R^5 and R^6 are attached, $(CH_2)_n$aryl wherein n is zero, 1, 2 or 3, heterocyclic or heteroaryl;

(d) when X is S and W is NH, then at least one of R^1, R^2, R^3, R^8 and R^9 is other than H or C_1-C_3 alkyl.

56. A compound of Claim 55 having the formula



58. A pharmaceutical formulation comprising a compound of Formula I



I

or a pharmaceutically acceptable salt thereof,
wherein:
the dotted line represents an optional double bond;
W is NH, S, SO, or SO_2;

X is either O, S, or NR^{10};
R^1, R^2, and R^{10} are independently selected from the group consisting of H, $(CH_2)_n$Ar, COR^4, $(CH_2)_n$heteroaryl, $(CH_2)_n$heterocyclyl, C_1-C_{10} alkyl, C_3-C_{10} cycloalkyl, C_2-C_{10} alkenyl, and C_2-C_{10} alkynyl, wherein n is 0, 1, 2, or 3, and

the $(CH_2)_nAr$, $(CH_2)_n$heteroaryl, alkyl, cycloalkyl, alkenyl, and alkynyl groups are optionally substituted by up to 5 groups selected from NR^4R^5, $N^+(O)R^4R^5$, $N^+R^4R^5R^6Y^-$, alkyl, phenyl, substituted phenyl, $(CH_2)_n$heteroaryl, hydroxy, alkoxy, phenoxy, thiol, thioalkyl, halo, COR^4, CO_2R^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4, aldehyde, nitrile, nitro,

heteroaryloxy,
$T(CH_2)_mQR^4$,

$$\begin{array}{l} OR^5 \\ | \\ T(CH_2)_mC\text{-}(CH_2)_mQR^4, \\ | \\ H \end{array}$$

$C(O)T(CH_2)_mQR^4$, $NHC(O)T(CH_2)_mQR^4$, $T(CH_2)_mC(O)NR^4NR^5$, and $T(CH_2)_mCO_2R^4$ wherein each m is independently 1-6, T is O, S, NR^4, $N^+(O)R^4$, $N^+R^4R^6Y^-$, or CR^4R^5, and Q is O, S, NR^5, $N^+(O)R^5$ or $N^+R^5R^6Y^-$;

and additionally alkyl, alkenyl and alkynyl can be further substituted with one to three cycloalkyl groups,

when the dotted line is present, R^3 is absent;
otherwise R^3 has the meanings of R^2, wherein R^2 is as defined above, as well as OH, NR^4R^5, $COOR^4$, OR^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4,

$$\begin{array}{l} OR^5 \\ | \\ T(CH_2)_mQR^4, \text{ or } T(CH_2)_mC\text{-}(CH_2)_mQR^4, \\ | \\ H \end{array}$$

wherein T and Q are as defined above;
R^4 and R^5 are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, substituted alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $N(C_1\text{-}C_6\text{alkyl})_{1 \text{ or } 2}$, $(CH_2)_nAr$, C_3-C_{10} cycloalkyl, heterocyclyl, and

heteroaryl, or R^4 and R^5 together with the nitrogen to which they are attached optionally form a ring having 3 to 7 carbon atoms and said ring optionally contains 1, 2, or 3 heteroatoms selected from the group consisting of nitrogen, substituted nitrogen, oxygen, and sulfur;

when R^4 and R^5 together with the nitrogen to which they are attached form a ring, the said ring is optionally substituted by 1 to 3 groups selected from OH, OR^4, NR^4R^5, $(CH_2)_mOR^4$, $(CH_2)_mNR^4R^5$, $T\text{-}(CH_2)_mQR_4$, $CO\text{-}T\text{-}(CH_2)_mQR^4$, $NH(CO)T(CH_2)_mQR^4$, $T\text{-}(CH_2)_mCO_2R^4$, and $T(CH_2)_mCONR^4R^5$;

R^6 is alkyl;

R^8 and R^9 independently are H, NR^4R^5, $N^+(O)R^4R^5$, $N^+R^4R^5R^6Y^-$, COR^4, CO_2R^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4, CN or nitro;

when the dotted line is absent, R^9 can additionally be = NOH,

= NOalkyl , =NOalkenyl, =NOalkynyl or =NOcycloalkyl;

and

Y is a halo counter-ion;

with the proviso that: (a) when R^8 and R^9 are both hydrogen, W is NH, R^1 is hydrogen and X is NR^{10}, then R^{10} is neither unsubstituted (C_1-C_{10}) alkyl, unsubstituted (C_2-C_{10}) alkenyl nor unsubstituted (C_2-C_{10}) alkynyl; and

(b) when R^8 or R^9 is NR^4R^5, $N^+(O)R^4R^5$, $N^+R^4R^5R^6Y^-$, COR^4, CO_2R^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4 or PO_3R^4, then one or more of R^4, R^5 and R^6 must be, independent of the nitrogen to which said one or more of R^4, R^5 and R^6 is attached, $(CH_2)_n$aryl wherein n is zero, 1, 2, or 3, heterocyclic or heteroaryl;

(c) when X is S and W is NH, then at least one of R^1, R^2, R^3, R^8 and R^9 is other than H or C_1-C_3 alkyl;

in combination with a pharmaceutically acceptable carrier, diluent, or excipient.

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANTS: ELLEN M. DOBRUSIN, ET AL.	:	EXAMINER: T. TRUONG
SERIAL NO. 09/623,737	:	ART UNIT: 1624
FILED: SEPTEMBER 7, 2000	:	PAPER NO.
FOR: BICYCLIC PYRIMIDINES AND BICYCLIC 3,4-DIHYDROPYRIMIDINES AS INHIBITORS OF CELLULAR PROLIFERATION	:	

Commissioner for Patents
Washington, D.C. 20231

CONTINGENT AMENDMENT

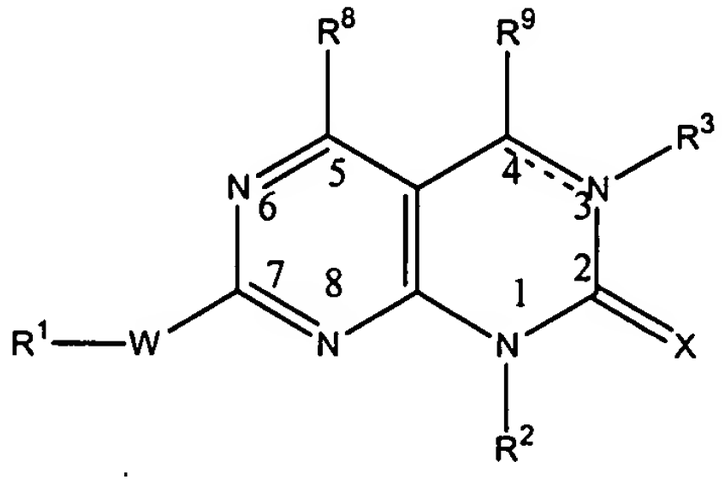
Dear Sir:

Contingent on the APJ in interference 104,798 determining that Dobrusin's claims 54, 55 and 58 are unpatentable, and Dobrusin's Count 2 is substituted for Count 1, please amend the above identified application as follows:

In the Claims:

Please add the following new claims:

- 77. A compound of Formula I



or a pharmaceutically acceptable salt thereof,
wherein:

the dotted line represents an optional double bond;
W is S, SO, or SO_2;

X is either O, S or NR^{10};
R^1, R^2, and R^{10} are independently selected from the group consisting of H, $(CH_2)_nAr$, COR^4, $(CH_2)_n$heteroaryl, $(CH_2)_n$heterocyclyl, C_1-C_{10} alkyl, C_3-C_{10} cycloalkyl, C_2-C_{10} alkenyl, and C_2-C_{10} alkynyl, wherein n is 0, 1, 2, or 3, and the $(CH_2)_nAr$, $(CH_2)_n$heteroaryl, alkyl, cycloalkyl, alkenyl, and alkynyl groups are optionally substituted by up to 5 groups selected from NR^4R^5, $N^+(O)R^4R^5$, $N^+R^4R^5R^6Y^-$, alkyl, phenyl, substituted phenyl, $(CH_2)_n$heteroaryl, hydroxy, alkoxy, phenoxy, thiol, thioalkyl, halo, COR^4, CO_2R^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4, aldehyde, nitrile, nitro,
heteroaryloxy,

$$T(CH_2)_mQR^4,\ T(CH_2)_mC(OR^5)H\text{-}(CH_2)_mQR^4,$$

$C(O)T(CH_2)_mQR^4$, $NHC(O)T(CH_2)_mQR^4$, $T(CH_2)_mC(O)NR^4NR^5$, and $T(CH_2)_mCO_2R^4$ wherein each m is independently 1-6, T is O, S, NR^4, $N^+(O)R^4$, $N^+R^4R^6Y^-$, or CR^4R^5, and Q is O, S, NR^5, $N^+(O)R^5$ or $N^+R^5R^6Y^-$;

and additionally alkyl, alkenyl and alkynyl can be further substituted with one to three cycloalkyl groups,

when the dotted line is present, R^3 is absent;
otherwise R^3 has the meanings of R^2, wherein R^2 is as defined above, as well as OH, NR^4R^5, $COOR^4$, OR^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4, $T(CH_2)_mQR^4$, or

$$T(CH_2)_mC(OR^5)H\text{-}(CH_2)_mQR^4,$$

wherein T and Q are as defined above;
R^4 and R^5 are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, substituted alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $N(C_1$-C_6alkyl$)_{1\text{ or }2}$, $(CH_2)_nAr$, C_3-C_{10} cycloalkyl, heterocyclyl, and

heteroaryl, or R^4 and R^5 together with the nitrogen to which they are attached optionally form a ring having 3 to 7 carbon atoms and said ring optionally contains 1, 2, or 3 heteroatoms selected from the group consisting of nitrogen, substituted nitrogen, oxygen, and sulfur;

when R^4 and R^5 together with the nitrogen to which they are attached form a ring, the said ring is optionally substituted by 1 to 3 groups selected from OH, OR^4, NR^4R^5, $(CH_2)_mOR^4$, $(CH_2)_mNR^4R^5$, $T\text{-}(CH_2)_mQR_4$, $CO\text{-}T\text{-}(CH_2)_mQR^4$, $NH(CO)T(CH_2)_mQR^4$, $T\text{-}(CH_2)_mCO_2R^4$, and $T(CH_2)_mCONR^4R^5$;

R^6 is alkyl;

R^8 and R^9 independently are H, CN or nitro;

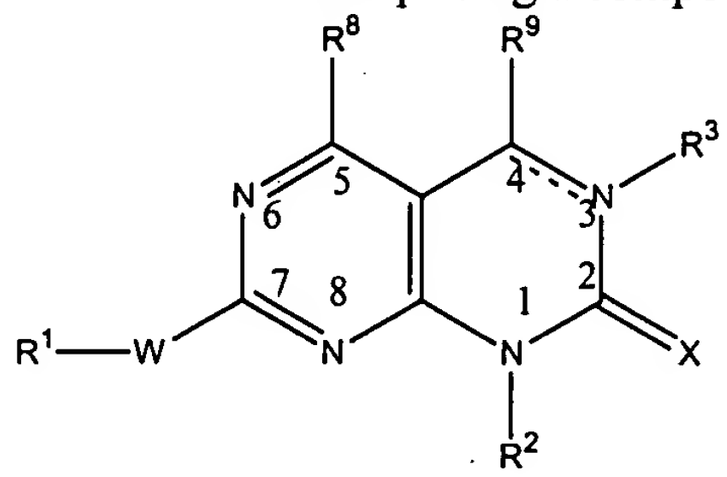
when the dotted line is absent, and R^9 is defined above, the carbon in the ring in the number 4 position that is bonded to R^9, is also bonded to a hydrogen atom,

when the dotted line is absent, R^9 can additionally be = NOH; and

Y is a halo counter-ion.

78. A compound of Claim 77, wherein R^8 and R^9 both are hydrogen.

79. A pharmaceutical formulation comprising a compound of Formula I



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or a pharmaceutically acceptable salt thereof,
wherein:
the dotted line represents an optional double bond;
W is S, SO, or SO_2;

X is either O, S or NR^{10};

R^1, R^2, and R^{10} are independently selected from the group consisting of H, $(CH_2)_nAr$, COR^4, $(CH_2)_n$heteroaryl, $(CH_2)_n$heterocyclyl, $C_1\text{-}C_{10}$ alkyl, $C_3\text{-}C_{10}$

cycloalkyl, C_2-C_{10} alkenyl, and C_2-C_{10} alkynyl, wherein n is 0, 1, 2, or 3, and the $(CH_2)_nAr$, $(CH_2)_n$heteroaryl, alkyl, cycloalkyl, alkenyl, and alkynyl groups are optionally substituted by up to 5 groups selected from NR^4R^5, $N^+(O)R^4R^5$, $N^+R^4R^5R^6Y^-$, alkyl, phenyl, substituted phenyl, $(CH_2)_n$heteroaryl, hydroxy, alkoxy, phenoxy, thiol, thioalkyl, halo, COR^4, CO_2R^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4, aldehyde, nitrile, nitro,

heteroaryloxy,
$T(CH_2)_mQR^4$,

$$T(CH_2)_mC\text{-}(CH_2)_mQR^4, \quad \begin{array}{c} OR^5 \\ | \\ \\ | \\ H \end{array}$$

$C(O)T(CH_2)_mQR^4$, $NHC(O)T(CH_2)_mQR^4$, $T(CH_2)_mC(O)NR^4NR^5$, and $T(CH_2)_mCO_2R^4$ wherein each m is independently 1-6, T is O, S, NR^4, $N^+(O)R^4$, $N^+R^4R^6Y^-$, or CR^4R^5, and Q is O, S, NR^5, $N^+(O)R^5$ or $N^+R^5R^6Y^-$;

and additionally alkyl, alkenyl and alkynyl can be further substituted with one to three cycloalkyl groups,

when the dotted line is present, R^3 is absent;
otherwise R^3 has the meanings of R^2, wherein R^2 is as defined above, as well as OH, NR^4R^5, $COOR^4$, OR^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4,

$$T(CH_2)_mQR^4, \text{ or } T(CH_2)_mC\text{-}(CH_2)_mQR^4, \quad \begin{array}{c} OR^5 \\ | \\ \\ | \\ H \end{array}$$

wherein T and Q are as defined above;
R^4 and R^5 are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, substituted alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl,

$N(C_1\text{-}C_6alkyl)_{1 \text{ or } 2}$, $(CH_2)_nAr$, $C_3\text{-}C_{10}$ cycloalkyl, heterocyclyl, and heteroaryl, or R^4 and R^5 together with the nitrogen to which they are attached optionally form a ring having 3 to 7 carbon atoms and said ring optionally contains 1, 2, or 3 heteroatoms selected from the group consisting of nitrogen, substituted nitrogen, oxygen, and sulfur;

when R^4 and R^5 together with the nitrogen to which they are attached form a ring, the said ring is optionally substituted by 1 to 3 groups selected from OH, OR^4, NR^4R^5, $(CH_2)_mOR^4$, $(CH_2)_mNR^4R^5$, $T\text{-}(CH_2)_mQR_4$, $CO\text{-}T\text{-}(CH_2)_mQR^4$, $NH(CO)T(CH_2)_mQR^4$, $T\text{-}(CH_2)_mCO_2R^4$, and $T(CH_2)_mCONR^4R^5$;

R^6 is alkyl;

R^8 and R^9 independently are H, CN or nitro;

when the dotted line is absent, and R^9 is defined above, the carbon in the ring in the number 4 position that is bonded to R^9, is also bonded to a hydrogen atom,

when the dotted line is absent, R^9 can additionally be = NOH;

and

Y is a halo counter-ion;

in combination with a pharmaceutically acceptable carrier, diluent, or excipient.

80. A formulation of Claim 79, wherein R^8 and R^9 both are hydrogen. - -

REMARKS

Dobrusin requests to add claims 77-80 to the interference, contingent on the APJ's determination that claims 54, 55 and 58 are unpatentable and Dobrusin's Count 2 is substituted for Count 1.

If there are any additional fees due in connection with the filing of this amendment, the applicants authorize the PTO to charge to Deposit Account No. 03-2775. A prompt and favorable action is solicited.

Respectfully submitted,

CONNOLLY BOVE LODGE & HUTZ LLP

By _____

Ashley I. Pezzner
Reg. No. 35,646
Tel. (302) 888-6270

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CERTIFICATE OF DELIVERY

I hereby certify that the **DOBRUSIN AMENDMENTS** are being filed by Express Mail with the U.S. Patent and Trademark Office, Board of Patent Appeals and Interferences, Crystal Gateway 2, 1225 Jefferson Davis Highway, Suite 1000, Arlington, Virginia 22202, on October 10, 2002.

J. Lynn Ferry

CERTIFICATE OF SERVICE

I hereby certify that a true copy of the foregoing **DOBRUSIN AMENDMENTS** are being served via Express Mail on October 10, 2002 upon Lead Counsel

Stephen M. Haracz, Esq.
Bryan Cave LLP
245 Park Avenue
New York, NY 10167-0034

and in-house counsel

George W. Johnston, Esq.
Hoffman LaRoche, Inc.
340 Kingsland Street
Nutley, New Jersey 07110-1199

J. Lynn Ferry

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANTS: ELLEN M. DOBRUSIN, ET AL.	:	EXAMINER: T. TRUONG
SERIAL NO. 09/623,737	:	ART UNIT: 1624
FILED: SEPTEMBER 7, 2000	:	PAPER NO.
FOR: BICYCLIC PYRIMIDINES AND BICYCLIC 3,4-DIHYDROPYRIMIDINES AS INHIBITORS OF CELLULAR PROLIFERATION	:	

Commissioner for Patents
Washington, D.C. 20231

CONTINGENT AMENDMENT

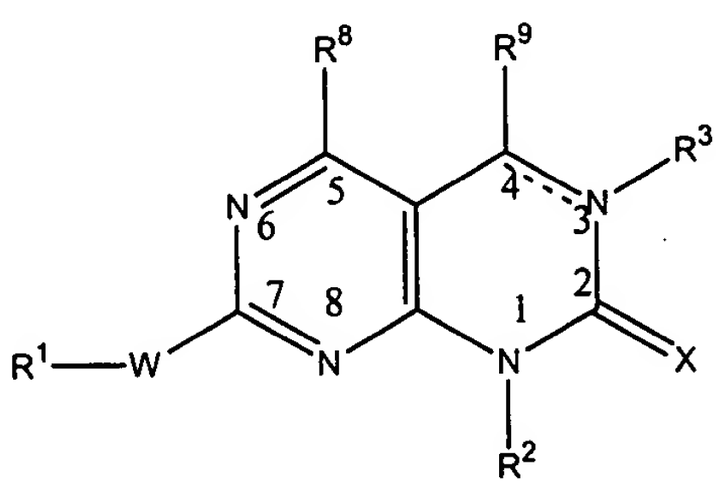
Dear Sir:

Contingent on the APJ in interference 104,798 determining that Dobrusin's claims 54, 55 and 58 are unpatentable, please amend the above identified application as follows:

In the Claims:

Please add the following new claims:

- - 61. A compound of Formula I



or a pharmaceutically acceptable salt thereof,
wherein:
the dotted line represents an optional double bond;
W is NH, S, SO, or SO_2;

X is either O or NR^{10};
R^1, R^2, and R^{10} are independently selected from the group consisting of H, $(CH_2)_nAr$, COR^4, $(CH_2)_n$heteroaryl, $(CH_2)_n$heterocyclyl, C_1-C_{10} alkyl, C_3-C_{10} cycloalkyl, C_2-C_{10} alkenyl, and C_2-C_{10} alkynyl, wherein n is 0, 1, 2, or 3, and the $(CH_2)_nAr$, $(CH_2)_n$heteroaryl, alkyl, cycloalkyl, alkenyl, and alkynyl groups are optionally substituted by up to 5 groups selected from NR^4R^5, $N^+(O)R^4R^5$, $N^+R^4R^5R^6Y^-$, alkyl, phenyl, substituted phenyl, $(CH_2)_n$heteroaryl, hydroxy, alkoxy, phenoxy, thiol, thioalkyl, halo, COR^4, CO_2R^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4, aldehyde, nitrile, nitro,
heteroaryloxy,

$$T(CH_2)_mQR^4,\ T(CH_2)_mC(OR^5)H\text{-}(CH_2)_mQR^4,$$

$C(O)T(CH_2)_mQR^4$, $NHC(O)T(CH_2)_mQR^4$, $T(CH_2)_mC(O)NR^4NR^5$, and $T(CH_2)_mCO_2R^4$ wherein each m is independently 1-6, T is O, S, NR^4, $N^+(O)R^4$, $N^+R^4R^6Y^-$, or CR^4R^5, and Q is O, S, NR^5, $N^+(O)R^5$ or $N^+R^5R^6Y^-$;

and additionally alkyl, alkenyl and alkynyl can be further substituted with one to three cycloalkyl groups,

when the dotted line is present, R^3 is absent;
otherwise R^3 has the meanings of R^2, wherein R^2 is as defined above, as well as OH, NR^4R^5, $COOR^4$, OR^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4,
$T(CH_2)_mQR^4$, or

$$T(CH_2)_mC(OR^5)H\text{-}(CH_2)_mQR^4,$$

wherein T and Q are as defined above;
R^4 and R^5 are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, substituted alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $N(C_1$-C_6alkyl$)_{1\text{ or }2}$, $(CH_2)_nAr$, C_3-C_{10} cycloalkyl, heterocyclyl, and heteroaryl, or R^4 and R^5 together with the nitrogen to which they are attached optionally form a ring having 3 to 7 carbon atoms and said ring optionally

contains 1, 2, or 3 heteroatoms selected from the group consisting of nitrogen, substituted nitrogen, oxygen, and sulfur;

when R^4 and R^5 together with the nitrogen to which they are attached form a ring, the said ring is optionally substituted by 1 to 3 groups selected from OH, OR^4, NR^4R^5, $(CH_2)_mOR^4$, $(CH_2)_mNR^4R^5$, $T\text{-}(CH_2)_mQR_4$, $CO\text{-}T\text{-}(CH_2)_mQR^4$, $NH(CO)T(CH_2)_mQR^4$, $T\text{-}(CH_2)_mCO_2R^4$, and $T(CH_2)_mCONR^4R^5$;

R^6 is alkyl;

R^8 and R^9 independently are H, NR^4R^5, $N^+(O)R^4R^5$, $N^+R^4R^5R^6Y^-$, COR^4, CO_2R^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4, CN or nitro;

when the dotted line is absent, and R^9 is defined above, the carbon in the ring in the number 4 position that is bonded to R^9, is also bonded to a hydrogen atom,

when the dotted line is absent, R^9 can additionally be = NOH;

and

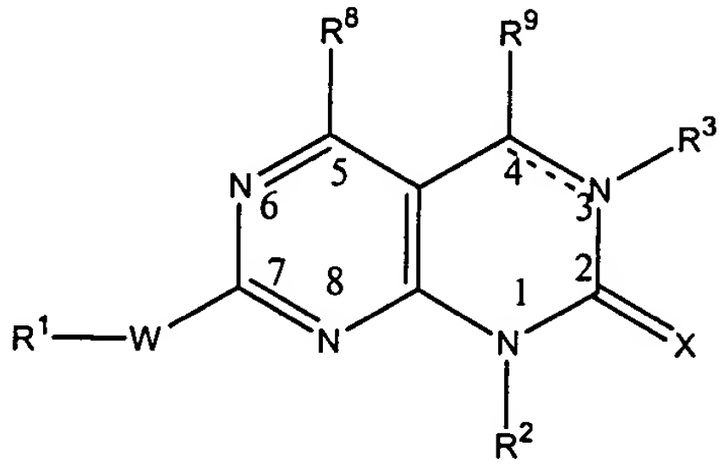
Y is a halo counter-ion;

with the proviso that: (a) when R^8 and R^9 are both hydrogen, W is NH, R^1 is hydrogen and X is NR^{10}, then R^{10} is neither unsubstituted $(C_1\text{-}C_{10})$ alkyl, unsubstituted $(C_2\text{-}C_{10})$ alkenyl nor unsubstituted $(C_2\text{-}C_{10})$ alkynyl;

(b) when R^8 or R^9 is NR^4R^5, $N^+(O)R^4R^5$, or $N^+R^4R^5R^6Y^-$, then one or more of R^4, R^5 and R^6 must be, independent of the nitrogen to which said one or more R^4, R^5 and R^6 are attached, heterocyclic or heteroaryl; and

(c) when R^8 or R^9 is COR^4, CO_2R^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4 or PO_3R^4, then one or more of R^4, R^5 and R^6 must be, independent of the nitrogen to which said one or more R^4, R^5 and R^6 are attached, $(CH_2)_n$aryl wherein n is zero, 1, 2 or 3, heterocyclic or heteroaryl.

62. A compound of Formula I



or a pharmaceutically acceptable salt thereof,
wherein:
the dotted line represents an optional double bond;
W is NH, S, SO, or SO_2;

X is either O or NR^{10};
R^1, R^2, and R^{10} are independently selected from the group consisting of H, $(CH_2)_nAr$, COR^4, $(CH_2)_n$heteroaryl, $(CH_2)_n$heterocyclyl, C_1-C_{10} alkyl, C_3-C_{10} cycloalkyl, C_2-C_{10} alkenyl, and C_2-C_{10} alkynyl, wherein n is 0, 1, 2, or 3, and the $(CH_2)_nAr$, $(CH_2)_n$heteroaryl, alkyl, cycloalkyl, alkenyl, and alkynyl groups are optionally substituted by up to 5 groups selected from NR^4R^5, $N^+(O)R^4R^5$, $N^+R^4R^5R^6Y^-$, alkyl, phenyl, substituted phenyl, $(CH_2)_n$heteroaryl, hydroxy, alkoxy, phenoxy, thiol, thioalkyl, halo, COR^4, CO_2R^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4, aldehyde, nitrile, nitro,
heteroaryloxy,

$$T(CH_2)_mQR^4,\ T(CH_2)_mC(OR^5)H\text{-}(CH_2)_mQR^4,$$

$C(O)T(CH_2)_mQR^4$, $NHC(O)T(CH_2)_mQR^4$, $T(CH_2)_mC(O)NR^4NR^5$, and $T(CH_2)_mCO_2R^4$ wherein each m is independently 1-6, T is O, S, NR^4, $N^+(O)R^4$, $N^+R^4R^6Y^-$, or CR^4R^5, and Q is O, S, NR^5, $N^+(O)R^5$ or $N^+R^5R^6Y^-$;

and additionally alkyl, alkenyl and alkynyl can be further substituted with one to three cycloalkyl groups,

when the dotted line is present, R^3 is absent;
otherwise R^3 has the meanings of R^2, wherein R^2 is as defined above, as well as OH, NR^4R^5, $COOR^4$, OR^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4, $T(CH_2)_mQR^4$, or

$$T(CH_2)_mC(OR^5)H\text{-}(CH_2)_mQR^4,$$

wherein T and Q are as defined above;
R^4 and R^5 are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, substituted alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $N(C_1$-C_6alkyl)$_{1 \text{ or } 2}$, $(CH_2)_nAr$, C_3-C_{10} cycloalkyl, heterocyclyl, and heteroaryl, or R^4 and R^5 together with the nitrogen to which they are attached optionally form a ring having 3 to 7 carbon atoms and said ring optionally contains 1, 2, or 3 heteroatoms selected from the group consisting of nitrogen, substituted nitrogen, oxygen, and sulfur;
when R^4 and R^5 together with the nitrogen to which they are attached form a ring, the said ring is optionally substituted by 1 to 3 groups selected from OH, OR^4, NR^4R^5, $(CH_2)_mOR^4$, $(CH_2)_mNR^4R^5$, T-$(CH_2)_mQR_4$, CO-T-$(CH_2)_mQR^4$, NH(CO)T$(CH_2)_mQR^4$, T-$(CH_2)_mCO_2R^4$, and $T(CH_2)_mCONR^4R^5$;
R^6 is alkyl;
R^8 and R^9 independently are H, CN or nitro;

when the dotted line is absent, and R^9 is defined above, the carbon in the ring in the number 4 position that is bonded to R^9, is also bonded to a hydrogen atom,

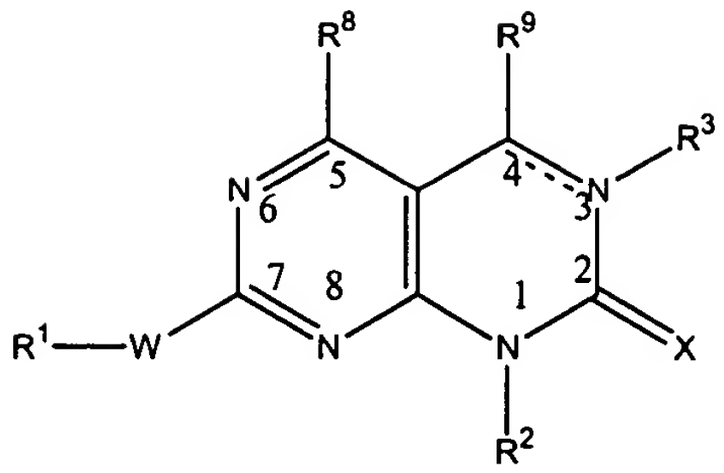
when the dotted line is absent, R^9 can additionally be = NOH;

and

Y is a halo counter-ion;

with the proviso that: (a) when R^8 and R^9 are both hydrogen, W is NH, R^1 is hydrogen and X is NR^{10}, then R^{10} is neither unsubstituted (C_1-C_{10}) alkyl, unsubstituted (C_2-C_{10}) alkenyl nor unsubstituted (C_2-C_{10}) alkynyl.

63. A compound of Formula I



or a pharmaceutically acceptable salt thereof,
wherein:
the dotted line represents an optional double bond;
W is NH, S, SO, or SO_2;
X is either O, S, or NR^{10};

R^1 is independently selected from the group consisting of $(CH_2)_nAr$, COR^4, $(CH_2)_n$heteroaryl, $(CH_2)_n$heterocyclyl, C_3-C_{10} cycloalkyl,C_2-C_{10} alkenyl, and C_2-C_{10} alkynyl, wherein n is 0, 1, 2, or 3, and the $(CH_2)_nAr$, $(CH_2)_n$heteroaryl, cycloalkyl, alkenyl, and alkynyl groups are optionally substituted by up to 5 groups selected from NR^4R^5, $N^+(O)R^4R^5$, $N^+R^4R^5R^6Y^-$, alkyl, phenyl, substituted phenyl, $(CH_2)_n$heteroaryl, hydroxy, alkoxy, phenoxy, thiol, thioalkyl, halo, COR^4, CO_2R^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4, aldehyde, nitrile, nitro,
heteroaryloxy,

$$T(CH_2)_mQR^4,\ T(CH_2)_mC(OR^5)(H)-(CH_2)_mQR^4,$$

$C(O)T(CH_2)_mQR^4$, $NHC(O)T(CH_2)_mQR^4$, $T(CH_2)_mC(O)NR^4NR^5$, and $T(CH_2)_mCO_2R^4$ wherein each m is independently 1-6, T is O, S, NR^4, $N^+(O)R^4$, $N^+R^4R^6Y^-$, or CR^4R^5, and Q is O, S, NR^5, $N^+(O)R^5$ or $N^+R^5R^6Y^-$;

R^2, and R^{10} are independently selected from the group consisting of H, $(CH_2)_nAr$, COR^4, $(CH_2)_n$heteroaryl, $(CH_2)_n$heterocyclyl, C_1-C_{10} alkyl, C_3-C_{10} cycloalkyl, C_2-C_{10} alkenyl, and C_2-C_{10} alkynyl, wherein n is 0, 1, 2, or 3, and the $(CH_2)_nAr$, $(CH_2)_n$heteroaryl, alkyl, cycloalkyl, alkenyl, and alkynyl groups are optionally substituted by up to 5 groups selected from NR^4R^5, $N^+(O)R^4R^5$,

$N^+R^4R^5R^6Y^-$, alkyl, phenyl, substituted phenyl, $(CH_2)_n$heteroaryl, hydroxy, alkoxy, phenoxy, thiol, thioalkyl, halo, COR^4, CO_2R^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4, aldehyde, nitrile, nitro,
heteroaryloxy,

$$T(CH_2)_mQR^4,\ T(CH_2)_mC(OR^5)H\text{-}(CH_2)_mQR^4,$$

$C(O)T(CH_2)_mQR^4$, $NHC(O)T(CH_2)_mQR^4$, $T(CH_2)_mC(O)NR^4NR^5$, and $T(CH_2)_mCO_2R^4$ wherein each m is independently 1-6, T is O, S, NR^4, $N^+(O)R^4$, $N^+R^4R^6Y^-$, or CR^4R^5, and Q is O, S, NR^5, $N^+(O)R^5$ or $N^+R^5R^6Y^-$;

and additionally alkyl, alkenyl and alkynyl can be further substituted with one to three cycloalkyl groups,

when the dotted line is present, R^3 is absent;
otherwise R^3 has the meanings of R^2, wherein R^2 is as defined above, as well as OH, NR^4R^5, $COOR^4$, OR^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4,
$T(CH_2)_mQR^4$, or

$$T(CH_2)_mC(OR^5)H\text{-}(CH_2)_mQR^4,$$

wherein T and Q are as defined above;
R^4 and R^5 are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, substituted alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $N(C_1\text{-}C_6alkyl)_{1\text{ or }2}$, $(CH_2)_nAr$, C_3-C_{10} cycloalkyl, heterocyclyl, and heteroaryl, or R^4 and R^5 together with the nitrogen to which they are attached optionally form a ring having 3 to 7 carbon atoms and said ring optionally contains 1, 2, or 3 heteroatoms selected from the group consisting of nitrogen, substituted nitrogen, oxygen, and sulfur;
when R^4 and R^5 together with the nitrogen to which they are attached form a ring, the said ring is optionally substituted by 1 to 3 groups selected from OH, OR^4, NR^4R^5, $(CH_2)_mOR^4$, $(CH_2)_mNR^4R^5$, $T\text{-}(CH_2)_mQR_4$,

$CO\text{-}T\text{-}(CH_2)_mQR^4$, $NH(CO)T(CH_2)_mQR^4$, $T\text{-}(CH_2)_mCO_2R^4$, and $T(CH_2)_mCONR^4R^5$;

R^6 is alkyl;

R^8 and R^9 independently are H, CN or nitro;

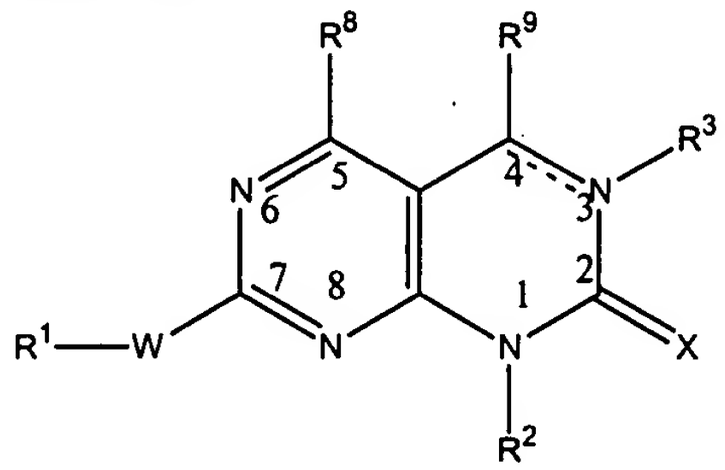
when the dotted line is absent, and R^9 is defined above, the carbon in the ring in the number 4 position that is bonded to R^9, is also bonded to a hydrogen atom,

when the dotted line is absent, R^9 can additionally be = NOH;

and

Y is a halo counter-ion.

64. A compound of Formula I



or a pharmaceutically acceptable salt thereof, wherein:

the dotted line represents an optional double bond;

W is NH, S, SO, or SO_2;

X is either O, or NR^{10};

R^1 and R^2 are independently selected from the group consisting of H, $(CH_2)_nAr$, COR^4, $(CH_2)_n$heteroaryl, $(CH_2)_n$heterocyclyl, C_1-C_{10} alkyl, C_3-C_{10} cycloalkyl, C_2-C_{10} alkenyl, and C_2-C_{10} alkynyl, wherein n is 0, 1, 2, or 3, and the $(CH_2)_nAr$, $(CH_2)_n$heteroaryl, alkyl, cycloalkyl, alkenyl, and alkynyl groups are optionally substituted by up to 5 groups selected from NR^4R^5, $N^+(O)R^4R^5$, $N^+R^4R^5R^6Y^-$, alkyl, phenyl, substituted phenyl, $(CH_2)_n$heteroaryl, hydroxy, alkoxy, phenoxy, thiol, thioalkyl, halo, COR^4, CO_2R^4, $CONR^4R^5$, $SO_2NR^4R^5$,

SO_3R^4, PO_3R^4, aldehyde, nitrile, nitro,
heteroaryloxy,

$$T(CH_2)_mQR^4,\ T(CH_2)_mC(OR^5)H\text{-}(CH_2)_mQR^4,$$

$C(O)T(CH_2)_mQR^4$, $NHC(O)T(CH_2)_mQR^4$, $T(CH_2)_mC(O)NR^4NR^5$, and $T(CH_2)_mCO_2R^4$ wherein each m is independently 1-6, T is O, S, NR^4, $N^+(O)R^4$, $N^+R^4R^6Y^-$, or CR^4R^5, and Q is O, S, NR^5, $N^+(O)R^5$ or $N^+R^5R^6Y^-$;
and additionally alkyl, alkenyl and alkynyl can be further substituted with one to three cycloalkyl groups,

R^{10} is selected from the group consisting of H, $(CH_2)_nAr$, COR^4, $(CH_2)_n$heteroaryl, $(CH_2)_n$heterocyclyl, C_3-C_{10} cycloalkyl, substituted C_1-C_{10} alkyl substituted by up to 5 substituents, substituted C_2-C_{10} alkenyl substituted by up to 5 substituents, and substituted C_2-C_{10} alkynyl substituted by up to 5 substituents,
wherein n is 0, 1, 2, or 3, and the $(CH_2)_nAr$, $(CH_2)_n$heteroaryl and cycloalkyl, groups are optionally substituted, by up to 5 substituents, wherein said substituents are selected from the group consisting of NR^4R^5, $N^+(O)R^4R^5$, $N^+R^4R^5R^6Y^-$, alkyl, phenyl, substituted phenyl, $(CH_2)_n$heteroaryl, hydroxy, alkoxy, phenoxy, thiol, thioalkyl, halo, COR^4, CO_2R^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4, aldehyde, nitrile, nitro,
heteroaryloxy,

$$T(CH_2)_mQR^4,\ T(CH_2)_mC(OR^5)H\text{-}(CH_2)_mQR^4,$$

$C(O)T(CH_2)_mQR^4$, $NHC(O)T(CH_2)_mQR^4$, $T(CH_2)_mC(O)NR^4NR^5$, and $T(CH_2)_mCO_2R^4$ wherein each m is independently 1-6, T is O, S, NR^4, $N^+(O)R^4$, $N^+R^4R^6Y^-$, or CR^4R^5, and Q is O, S, NR^5, $N^+(O)R^5$ or $N^+R^5R^6Y^-$;

and additionally alkyl, alkenyl and alkynyl can be further substituted with one to three cycloalkyl groups,

when the dotted line is present, R^3 is absent;
otherwise R^3 has the meanings of R^2, wherein R^2 is as defined above, as well as OH, NR^4R^5, $COOR^4$, OR^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4,
$T(CH_2)_mQR^4$, or

$$T(CH_2)_mC(OR^5)(H)-(CH_2)_mQR^4,$$

wherein T and Q are as defined above;
R^4 and R^5 are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, substituted alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $N(C_1$-C_6alkyl$)_{1 \text{ or } 2}$, $(CH_2)_nAr$, C_3-C_{10} cycloalkyl, heterocyclyl, and heteroaryl, or R^4 and R^5 together with the nitrogen to which they are attached optionally form a ring having 3 to 7 carbon atoms and said ring optionally contains 1, 2, or 3 heteroatoms selected from the group consisting of nitrogen, substituted nitrogen, oxygen, and sulfur;
when R^4 and R^5 together with the nitrogen to which they are attached form a ring, the said ring is optionally substituted by 1 to 3 groups selected from OH, OR^4, NR^4R^5, $(CH_2)_mOR^4$, $(CH_2)_mNR^4R^5$, T-$(CH_2)_mQR_4$, CO-T-$(CH_2)_mQR^4$, $NH(CO)T(CH_2)_mQR^4$, T-$(CH_2)_mCO_2R^4$, and $T(CH_2)_mCONR^4R^5$;
R^6 is alkyl;
R^8 and R^9 independently are H, CN or nitro;

when the dotted line is absent, and R^9 is defined above, the carbon in the ring in the number 4 position that is bonded to R^9, is also bonded to a hydrogen atom,

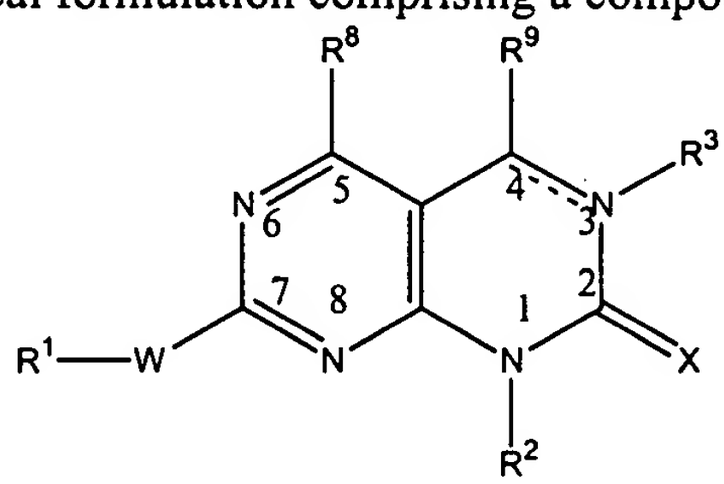
when the dotted line is absent, R^9 can additionally be = NOH;

and

Y is a halo counter-ion.

65. A compound of Claim 61, wherein W is NH, and R^8 and R^9 both are hydrogen.
66. A compound of Claim 62, wherein W is NH, and R^8 and R^9 both are hydrogen.
67. A compound of Claim 63, wherein W is NH, and R^8 and R^9 both are hydrogen.
68. A compound of Claim 64, wherein W is NH , and R^8 and R^9 both are hydrogen.

69. A pharmaceutical formulation comprising a compound of Formula I



I

or a pharmaceutically acceptable salt thereof,
wherein:
the dotted line represents an optional double bond;
W is NH, S, SO, or SO_2;

X is either O, or NR^{10};
R^1, R^2, and R^{10} are independently selected from the group consisting of H, $(CH_2)_nAr$, COR^4, $(CH_2)_n$heteroaryl, $(CH_2)_n$heterocyclyl, C_1-C_{10} alkyl, C_3-C_{10} cycloalkyl, C_2-C_{10} alkenyl, and C_2-C_{10} alkynyl, wherein n is 0, 1, 2, or 3, and the $(CH_2)_nAr$, $(CH_2)_n$heteroaryl, alkyl, cycloalkyl, alkenyl, and alkynyl groups are optionally substituted by up to 5 groups selected from NR^4R^5, $N^+(O)R^4R^5$, $N^+R^4R^5R^6Y^-$, alkyl, phenyl, substituted phenyl, $(CH_2)_n$heteroaryl, hydroxy, alkoxy, phenoxy, thiol, thioalkyl, halo, COR^4, CO_2R^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4, aldehyde, nitrile, nitro,
heteroaryloxy, $T(CH_2)_mQR^4$,

$$T(CH_2)_mC(OR^5)H\text{-}(CH_2)_mQR^4,$$

$C(O)T(CH_2)_mQR^4$, $NHC(O)T(CH_2)_mQR^4$, $T(CH_2)_mC(O)NR^4NR^5$, and $T(CH_2)_mCO_2R^4$ wherein each m is independently 1-6, T is O, S, NR^4, $N^+(O)R^4$, $N^+R^4R^6Y^-$, or CR^4R^5, and Q is O, S, NR^5, $N^+(O)R^5$ or $N^+R^5R^6Y^-$;

and additionally alkyl, alkenyl and alkynyl can be further substituted with one to three cycloalkyl groups,

when the dotted line is present, R^3 is absent;
otherwise R^3 has the meanings of R^2, wherein R^2 is as defined above, as well as OH, NR^4R^5, $COOR^4$, OR^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4,

$$T(CH_2)_mQR^4, \text{ or } T(CH_2)_mC(OR^5)(H)-(CH_2)_mQR^4,$$

wherein T and Q are as defined above;
R^4 and R^5 are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, substituted alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $N(C_1$-C_6alkyl$)_{1 \text{ or } 2}$, $(CH_2)_nAr$, C_3-C_{10} cycloalkyl, heterocyclyl, and heteroaryl, or R^4 and R^5 together with the nitrogen to which they are attached optionally form a ring having 3 to 7 carbon atoms and said ring optionally contains 1, 2, or 3 heteroatoms selected from the group consisting of nitrogen, substituted nitrogen, oxygen, and sulfur;
when R^4 and R^5 together with the nitrogen to which they are attached form a ring, the said ring is optionally substituted by 1 to 3 groups selected from OH, OR^4, NR^4R^5, $(CH_2)_mOR^4$, $(CH_2)_mNR^4R^5$, T-$(CH_2)_mQR_4$, CO-T-$(CH_2)_mQR^4$, $NH(CO)T(CH_2)_mQR^4$, T-$(CH_2)_mCO_2R^4$, and $T(CH_2)_mCONR^4R^5$;
R^6 is alkyl;
R^8 and R^9 independently are H, NR^4R^5, $N^+(O)R^4R^5$, $N^+R^4R^5R^6Y^-$, COR^4, CO_2R^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4, CN or nitro;

when the dotted line is absent, and R^9 is defined above, the carbon in the ring in the number 4 position that is bonded to R^9, is also bonded to a hydrogen atom,

when the dotted line is absent, R^9 can additionally be = NOH;

and

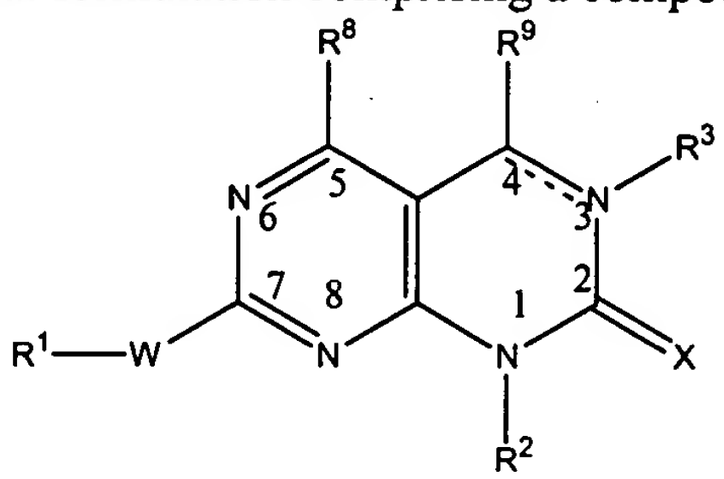
Y is a halo counter-ion;

with the proviso that: (a) when R^8 and R^9 are both hydrogen, W is NH, R^1 is hydrogen and X is NR^{10}, then R^{10} is neither unsubstituted (C_1-C_{10}) alkyl, unsubstituted (C_2-C_{10}) alkenyl nor unsubstituted (C_2-C_{10}) alkynyl; and

(b) when R^8 or R^9 is NR^4R^5, $N^+(O)R^4R^5$, $N^+R^4R^5R^6Y^-$, COR^4, CO_2R^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4 or PO_3R^4, then one or more of R^4, R^5 and R^6 must be, independent of the nitrogen to which said one or more of R^4, R^5 and R^6 is attached, $(CH_2)_n$aryl wherein n is zero, 1, 2, or 3, heterocyclic or heteroaryl;

in combination with a pharmaceutically acceptable carrier, diluent, or excipient.

70. A pharmaceutical formulation comprising a compound of Formula I



I

or a pharmaceutically acceptable salt thereof,
wherein:
the dotted line represents an optional double bond;
W is NH, S, SO, or SO_2;

X is either O, or NR^{10};

R^1, R^2, and R^{10} are independently selected from the group consisting of H, $(CH_2)_nAr$, COR^4, $(CH_2)_n$heteroaryl, $(CH_2)_n$heterocyclyl, C_1-C_{10} alkyl, C_3-C_{10} cycloalkyl, C_2-C_{10} alkenyl, and C_2-C_{10} alkynyl, wherein n is 0, 1, 2, or 3, and the $(CH_2)_nAr$, $(CH_2)_n$heteroaryl, alkyl, cycloalkyl, alkenyl, and alkynyl groups are optionally substituted by up to 5 groups selected from NR^4R^5, $N^+(O)R^4R^5$, $N^+R^4R^5R^6Y^-$, alkyl, phenyl, substituted phenyl, $(CH_2)_n$heteroaryl, hydroxy, alkoxy, phenoxy, thiol, thioalkyl, halo, COR^4, CO_2R^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4, aldehyde, nitrile, nitro,
heteroaryloxy, $T(CH_2)_mQR^4$,

$$T(CH_2)_mC\text{-}(CH_2)_mQR^4,$$
(with OR^5 and H substituents on the C)

$C(O)T(CH_2)_mQR^4$, $NHC(O)T(CH_2)_mQR^4$, $T(CH_2)_mC(O)NR^4NR^5$, and $T(CH_2)_mCO_2R^4$ wherein each m is independently 1-6, T is O, S, NR^4, $N^+(O)R^4$, $N^+R^4R^6Y^-$, or CR^4R^5, and Q is O, S, NR^5, $N^+(O)R^5$ or $N^+R^5R^6Y^-$;

and additionally alkyl, alkenyl and alkynyl can be further substituted with one to three cycloalkyl groups,

when the dotted line is present, R^3 is absent;
otherwise R^3 has the meanings of R^2, wherein R^2 is as defined above, as well as OH, NR^4R^5, $COOR^4$, OR^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4,

$$T(CH_2)_mQR^4, \text{ or } T(CH_2)_mC\text{-}(CH_2)_mQR^4,$$
(with OR^5 and H substituents on the C)

wherein T and Q are as defined above;
R^4 and R^5 are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, substituted alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $N(C_1\text{-}C_6\text{alkyl})_{1 \text{ or } 2}$, $(CH_2)_nAr$, C_3-C_{10} cycloalkyl, heterocyclyl, and heteroaryl, or R^4 and R^5 together with the nitrogen to which they are attached

optionally form a ring having 3 to 7 carbon atoms and said ring optionally contains 1, 2, or 3 heteroatoms selected from the group consisting of nitrogen, substituted nitrogen, oxygen, and sulfur;

when R^4 and R^5 together with the nitrogen to which they are attached form a ring, the said ring is optionally substituted by 1 to 3 groups selected from OH, OR^4, NR^4R^5, $(CH_2)_mOR^4$, $(CH_2)_mNR^4R^5$, $T\text{-}(CH_2)_mQR_4$, $CO\text{-}T\text{-}(CH_2)_mQR^4$, $NH(CO)T(CH_2)_mQR^4$, $T\text{-}(CH_2)_mCO_2R^4$, and $T(CH_2)_mCONR^4R^5$;

R^6 is alkyl;

R^8 and R^9 independently are H, CN or nitro;

when the dotted line is absent, and R^9 is defined above, the carbon in the ring in the number 4 position that is bonded to R^9, is also bonded to a hydrogen atom,

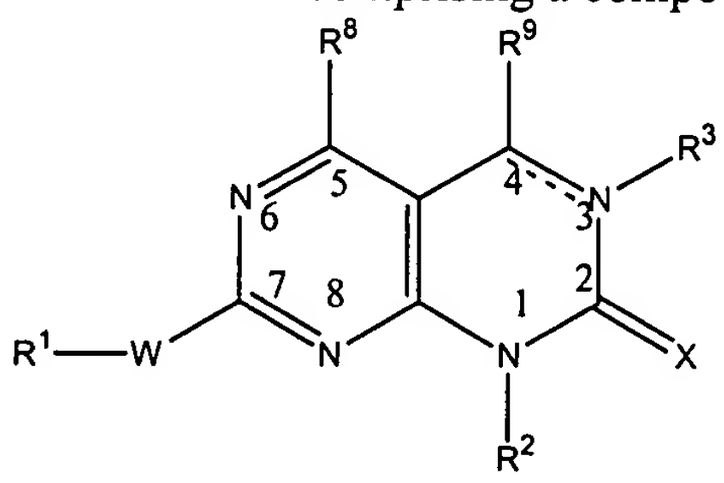
when the dotted line is absent, R^9 can additionally be = NOH; and

Y is a halo counter-ion;

with the proviso that: (a) when R^8 and R^9 are both hydrogen, W is NH, R^1 is hydrogen and X is NR^{10}, then R^{10} is neither unsubstituted (C_1-C_{10}) alkyl, unsubstituted (C_2-C_{10}) alkenyl nor unsubstituted (C_2-C_{10}) alkynyl; and

in combination with a pharmaceutically acceptable carrier, diluent, or excipient.

71. A pharmaceutical formulation comprising a compound of Formula I



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or a pharmaceutically acceptable salt thereof,

wherein:
the dotted line represents an optional double bond;
W is NH, S, SO, or SO_2;

X is either O, S or NR^{10};

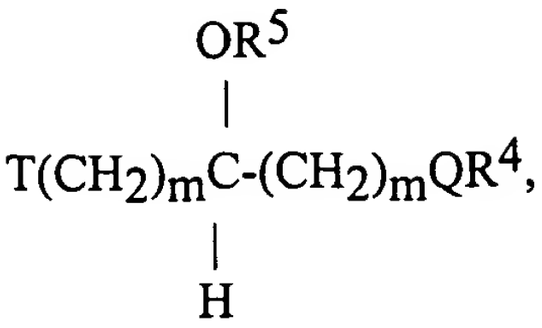
R^1 is independently selected from the group consisting of $(CH_2)_nAr$, COR^4, $(CH_2)_n$heteroaryl, $(CH_2)_n$heterocyclyl, C_3-C_{10} cycloalkyl,C_2-C_{10} alkenyl, and C_2-C_{10} alkynyl, wherein n is 0, 1, 2, or 3, and the $(CH_2)_nAr$, $(CH_2)_n$heteroaryl, cycloalkyl, alkenyl, and alkynyl groups are optionally substituted by up to 5 groups selected from NR^4R^5, $N^+(O)R^4R^5$, $N^+R^4R^5R^6Y^-$, alkyl, phenyl, substituted phenyl, $(CH_2)_n$heteroaryl, hydroxy, alkoxy, phenoxy, thiol, thioalkyl, halo, COR^4, CO_2R^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4, aldehyde, nitrile, nitro,
heteroaryloxy,

$$T(CH_2)_mQR^4,\ T(CH_2)_mC(OR^5)H\text{-}(CH_2)_mQR^4,$$

$C(O)T(CH_2)_mQR^4$, $NHC(O)T(CH_2)_mQR^4$, $T(CH_2)_mC(O)NR^4NR^5$, and $T(CH_2)_mCO_2R^4$ wherein each m is independently 1-6, T is O, S, NR^4, $N^+(O)R^4$, $N^+R^4R^6Y^-$, or CR^4R^5, and Q is O, S, NR^5, $N^+(O)R^5$ or $N^+R^5R^6Y^-$;

R^2, and R^{10} are independently selected from the group consisting of H, $(CH_2)_nAr$, COR^4, $(CH_2)_n$heteroaryl, $(CH_2)_n$heterocyclyl, C_1-C_{10} alkyl, C_3-C_{10} cycloalkyl, C_2-C_{10} alkenyl, and C_2-C_{10} alkynyl, wherein n is 0, 1, 2, or 3, and the $(CH_2)_nAr$, $(CH_2)_n$heteroaryl, alkyl, cycloalkyl, alkenyl, and alkynyl groups are optionally substituted by up to 5 groups selected from NR^4R^5, $N^+(O)R^4R^5$, $N^+R^4R^5R^6Y^-$, alkyl, phenyl, substituted phenyl, $(CH_2)_n$heteroaryl, hydroxy, alkoxy, phenoxy, thiol, thioalkyl, halo, COR^4, CO_2R^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4, aldehyde, nitrile, nitro,

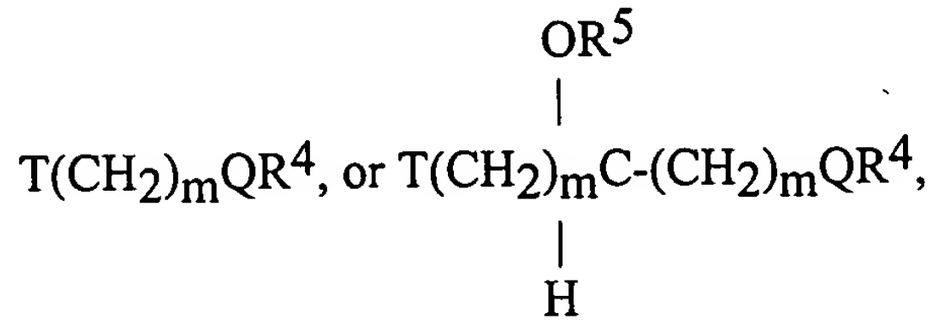
heteroaryloxy,
$T(CH_2)_mQR^4$,



$C(O)T(CH_2)_mQR^4$, $NHC(O)T(CH_2)_mQR^4$, $T(CH_2)_mC(O)NR^4NR^5$, and $T(CH_2)_mCO_2R^4$ wherein each m is independently 1-6, T is O, S, NR^4, $N^+(O)R^4$, $N^+R^4R^6Y^-$, or CR^4R^5, and Q is O, S, NR^5, $N^+(O)R^5$ or $N^+R^5R^6Y^-$;

and additionally alkyl, alkenyl and alkynyl can be further substituted with one to three cycloalkyl groups,

when the dotted line is present, R^3 is absent;
otherwise R^3 has the meanings of R^2, wherein R^2 is as defined above, as well as OH, NR^4R^5, $COOR^4$, OR^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4,



wherein T and Q are as defined above;
R^4 and R^5 are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, substituted alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $N(C_1$-C_6alkyl$)_{1 \text{ or } 2}$, $(CH_2)_nAr$, C_3-C_{10} cycloalkyl, heterocyclyl, and heteroaryl, or R^4 and R^5 together with the nitrogen to which they are attached optionally form a ring having 3 to 7 carbon atoms and said ring optionally contains 1, 2, or 3 heteroatoms selected from the group consisting of nitrogen, substituted nitrogen, oxygen, and sulfur;
when R^4 and R^5 together with the nitrogen to which they are attached form a ring, the said ring is optionally substituted by 1 to 3 groups selected from OH, OR^4, NR^4R^5, $(CH_2)_mOR^4$, $(CH_2)_mNR^4R^5$, T-$(CH_2)_mQR_4$, CO-T-$(CH_2)_mQR^4$, $NH(CO)T(CH_2)_mQR^4$, T-$(CH_2)_mCO_2R^4$, and $T(CH_2)_mCONR^4R^5$;
R^6 is alkyl;
R^8 and R^9 independently are H, CN or nitro;

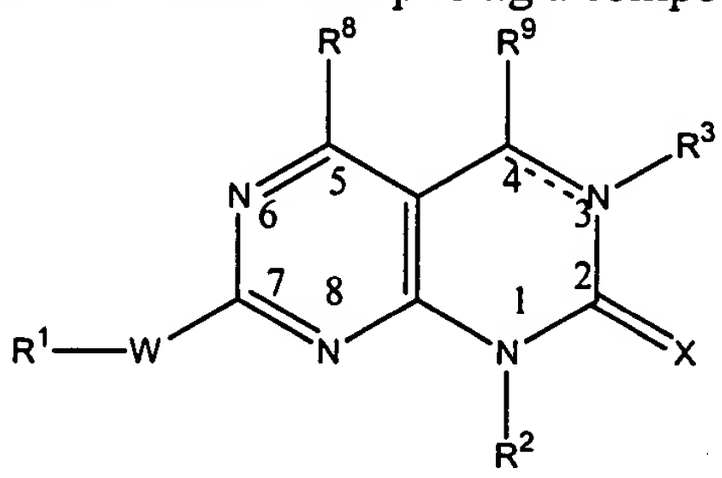
when the dotted line is absent, and R^9 is defined above, the carbon in the ring in the number 4 position that is bonded to R^9, is also bonded to a hydrogen atom,

when the dotted line is absent, R^9 can additionally be = NOH; and

Y is a halo counter-ion;

in combination with a pharmaceutically acceptable carrier, diluent, or excipient.

72. A pharmaceutical formulation comprising a compound of Formula I



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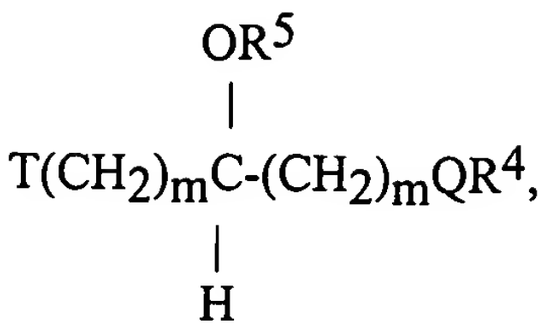
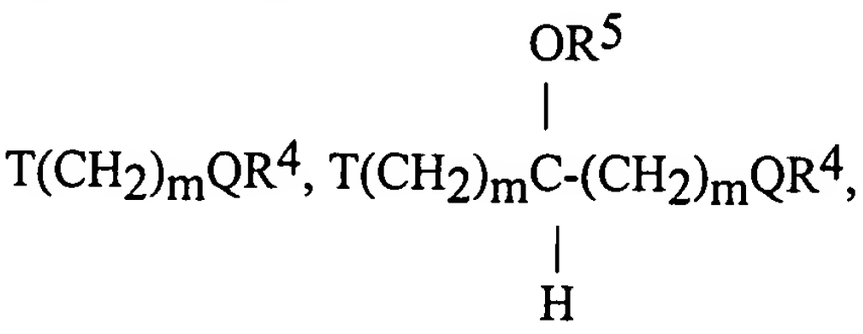
or a pharmaceutically acceptable salt thereof,
wherein:
the dotted line represents an optional double bond;
W is NH, S, SO, or SO_2;
X is either O, or NR^{10};
R^1, and R^2 are independently selected from the group consisting of H, $(CH_2)_nAr$, COR^4, $(CH_2)_n$heteroaryl, $(CH_2)_n$heterocyclyl, C_1-C_{10} alkyl, C_3-C_{10} cycloalkyl, C_2-C_{10} alkenyl, and C_2-C_{10} alkynyl, wherein n is 0, 1, 2, or 3, and the $(CH_2)_nAr$, $(CH_2)_n$heteroaryl, alkyl, cycloalkyl, alkenyl, and alkynyl groups are optionally substituted by up to 5 groups selected from NR^4R^5, $N^+(O)R^4R^5$, $N^+R^4R^5R^6Y^-$, alkyl, phenyl, substituted phenyl, $(CH_2)_n$heteroaryl, hydroxy, alkoxy, phenoxy, thiol, thioalkyl, halo, COR^4, CO_2R^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4, aldehyde, nitrile, nitro, heteroaryloxy, $T(CH_2)_mQR^4$,



$C(O)T(CH_2)_mQR^4$, $NHC(O)T(CH_2)_mQR^4$, $T(CH_2)_mC(O)NR^4NR^5$, and $T(CH_2)_mCO_2R^4$ wherein each m is independently 1-6, T is O, S, NR^4, $N^+(O)R^4$, $N^+R^4R^6Y^-$, or CR^4R^5, and Q is O, S, NR^5, $N^+(O)R^5$ or $N^+R^5R^6Y^-$;

R^{10} is selected from the group consisting of H, $(CH_2)_nAr$, COR^4, $(CH_2)_n$heteroaryl, $(CH_2)_n$heterocyclyl, C_3-C_{10} cycloalkyl, substituted C_1-C_{10} alkyl substituted by up to 5 substituents, substituted C_2-C_{10} alkenyl substituted by up to 5 substituents, and substituted C_2-C_{10} alkynyl substituted by up to 5 substituents,
wherein n is 0, 1, 2, or 3, and the $(CH_2)_nAr$, $(CH_2)_n$heteroaryl and cycloalkyl, groups are optionally substituted, by up to 5 substituents, wherein said substituents are selected from the group consisting of NR^4R^5, $N^+(O)R^4R^5$, $N^+R^4R^5R^6Y^-$, alkyl, phenyl, substituted phenyl, $(CH_2)_n$heteroaryl, hydroxy, alkoxy, phenoxy, thiol, thioalkyl, halo, COR^4, CO_2R^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4, aldehyde, nitrile, nitro,
heteroaryloxy,



$C(O)T(CH_2)_mQR^4$, $NHC(O)T(CH_2)_mQR^4$, $T(CH_2)_mC(O)NR^4NR^5$, and $T(CH_2)_mCO_2R^4$ wherein each m is independently 1-6, T is O, S, NR^4, $N^+(O)R^4$, $N^+R^4R^6Y^-$, or CR^4R^5, and Q is O, S, NR^5, $N^+(O)R^5$ or $N^+R^5R^6Y^-$;

and additionally alkyl, alkenyl and alkynyl can be further substituted with one to three cycloalkyl groups,

when the dotted line is present, R^3 is absent;

otherwise R^3 has the meanings of R^2, wherein R^2 is as defined above, as well as OH, NR^4R^5, $COOR^4$, OR^4, $CONR^4R^5$, $SO_2NR^4R^5$, SO_3R^4, PO_3R^4,

$$T(CH_2)_mQR^4, \text{ or } T(CH_2)_mC(OR^5)H\text{-}(CH_2)_mQR^4,$$

wherein T and Q are as defined above;

R^4 and R^5 are each independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, substituted alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, $N(C_1\text{-}C_6\text{alkyl})_{1 \text{ or } 2}$, $(CH_2)_nAr$, C_3-C_{10} cycloalkyl, heterocyclyl, and heteroaryl, or R^4 and R^5 together with the nitrogen to which they are attached optionally form a ring having 3 to 7 carbon atoms and said ring optionally contains 1, 2, or 3 heteroatoms selected from the group consisting of nitrogen, substituted nitrogen, oxygen, and sulfur;

when R^4 and R^5 together with the nitrogen to which they are attached form a ring, the said ring is optionally substituted by 1 to 3 groups selected from OH, OR^4, NR^4R^5, $(CH_2)_mOR^4$, $(CH_2)_mNR^4R^5$, $T\text{-}(CH_2)_mQR_4$, $CO\text{-}T\text{-}(CH_2)_mQR^4$, $NH(CO)T(CH_2)_mQR^4$, $T\text{-}(CH_2)_mCO_2R^4$, and $T(CH_2)_mCONR^4R^5$;

R^6 is alkyl;

R^8 and R^9 independently are H, CN or nitro;

when the dotted line is absent, and R^9 is defined above, the carbon in the ring in the number 4 position that is bonded to R^9, is also bonded to a hydrogen atom,

when the dotted line is absent, R^9 can additionally be = NOH; and

Y is a halo counter-ion;

in combination with a pharmaceutically acceptable carrier, diluent, or excipient.

73. A formulation of Claim 69, wherein W is NH, and R^8 and R^9 both are hydrogen.

74. A formulation of Claim 70, wherein W is NH, and R^8 and R^9 both are hydrogen.

75. A formulation of Claim 71, wherein W is NH, and R^8 and R^9 both are hydrogen.

76. A formulation of Claim 72, wherein W is NH, and R^8 and R^9 both are hydrogen. - -

REMARKS

Claims 61-76 are discussed in Dobrusin's Preliminary Motion no. 4. If the APJ determines that Dobrusin's claims 54, 55 and 58 are unpatentable, Dobrusin requests to add claims 61-76. If there are any additional fees due in connection with the filing of this amendment, the applicants authorize the PTO to charge to Deposit Account No. 03-2775. A prompt and favorable action is solicited.

Respectfully submitted,

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